Gene Engineering Division

Head
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Goal

The Gene Engineering Division (RIKEN DNA Bank) is a nonprofit resource archive that provides genetic resources, technical services and educational program to qualified investigators in private industries, governments and academic organizations around the world. RIKEN DNA Bank has been selected as a central facility for collecting, preserving and delivering DNAs of animals and microorganisms through the National BioResource Project sponsored by the Ministry of Education, Culture, Sports, Science and Technology of JAPAN (MEXT). Our division conducts research to ensure the authenticity of the genetic materials in the collection, and to improve and standardize the methods of characterization, maintenance, preservation and distribution of genetic materials. We distribute cloned DNAs, gene libraries (e.g., cDNAs, phages, cosmids, BAC, phosmids, and YAC libraries), vectors, hosts, recombinant viruses and ordered library sets from humans, mice, microorganisms, viruses and other animals. Our division also performs and sponsors research to improve and standardizes for the advancement, validation and application of scientific knowledge.

History

RIKEN DNA Bank was established in June 1987 when a committee of scientists recognized the need for a central collection of recombinant DNA that would serve scientists in Asia. In 2001, RIKEN BioResource Center (RIKEN BRC) was established and then the DNA Bank was reorganized into the Division of Gene Engineering. In 2002, the division was recognized as the central archive for the collection of “animal DNA and microorganism DNA” in the National BioResource Project (NBRP) program (Phase I), sponsored by MEXT. In 2007, it was also recognized as the central archive for the collection of “DNA” in the NBRP (Phase II), sponsored by MEXT.

Activities

1. Collection, preservation and distribution of genetic resources

The Gene Engineering Division (RIKEN DNA Bank) is divided into seven sections for DNA Banking.

(1) Cloned-DNA Set Bank. This handles a cloned collection of full-length cDNAs assembled with specific research areas such as hormones, cytokines, apoptosis, cell cycle, signal cascades, transcription factors, replication factors, and ubiquitination. These representative cloned sets were isolated from cDNA libraries, phage, cosmids, BAC, YAC, PAC, P1 and phosmid libraries.

(2) Japanese-Specific DNA Bank. This handles human HLA class I clones that are unique to Japanese and SEREX clones coding cancer antigens of Japanese origin and to other clones for Japanese heredity.

(3) Recombinant-Virus Bank. This handles recombinant viruses constructed by inserting a full-length cDNA into viral vectors, generating the viral particles as resources. The viruses are examined of their qualities by methods developed in our division. The DNA fragments derived from human and mouse full-length cDNA libraries were used as donors of recombinant viruses.

(4) Promoter Bank. This handles promoter DNA fragments fused to reporter genes such as luciferase, lacZ, GFP and Cre recombinase. Transgenic promoter Cre mice are also generated by collaborating with the Animal Resource Center of Tsukuba University and the Experimental Animal Division of RIKEN BRC. The second phase of
this Bank is to address the promoters of p53-related genes with reporter constructs.

(5) Archives of large-genome cloned library. This handles cDNA and genome libraries from various animals. This section was based on the NBRP for collecting all genome resources produced by the NBRP (Phases I and II) such as those from *Xenopus*, Japanese monkeys, rats, mice, humans, yeasts, *Ciona* and *Thermus thermophilus*.

(6) Basic domain of DNA Bank. This handles individual cDNAs, genome DNA clones and vectors as well as host cells.

(7) Bioinformatics section. This handles the informatics of our genetic resources for DNA Banking.

We distribute genetic resources to only qualified researchers associated with certain research, medical or educational organizations. We also report the activities of our division in an annual report, qualified by the “Resource Committee”. We also discuss the future plan of our mission. The “Resource Ethics Committee” confirms the banking activity of genetic resources of humans every year. The “Advisory Council” is held to evaluate the activities of RIKEN BRC every other year. We evaluate not only the activities of our DNA Banking but also the research activities of developing technologies related to DNA Banking.

2. Development of new technology to ensure the authenticity of genetic materials

The development and improvement of methods for the standardization and characterization of genetic resources are also conducted by our division. These technologies, as described below, are necessary and entail the following:

1) identification of mutation sites in genetic resources;
2) preparation of novel vectors and an adenovirus vector for the controlled expression system of genes;
3) preparation of an artificial reporter vector with different cis-elements and promoter-reporter constructs;
4) development and validation of new gene-transferring system using targeted promoter/enhancer element;
5) development of a new system for studying gene expression in eukaryotic cells and animals; and
6) production of modified proteins in *Escherichia coli* on a large scale.

3. Education and training of scientists.

Our division offers a training program for young scientists and students that teaches the best use of adenoviral vectors.
Specific Aims

I. Collection, preparation and distribution of genetic materials.

1. Banking system
We have collected the following numbers of genetic materials: host, vector, cloned DNA, 3,451; Nakamura-White RELP marker clone, 123; human genomic YAC clone library, 35,712; human full length cDNA cloned library, 307,200; mouse 15 K cDNA cloned library, 15,000; mouse 7.4 K cDNA cloned library, 7,407; mouse cDNA cloned library, 45,216; cDNA library, 47; mouse BAC cloned library, 193,152; human SEREX clone, 584; Japanese HLA class I, 40; recombinant virus, 502; NBRP Japanese macaque genome library, 200,064; Tokushima Univ. mouse cDNA cloned library, 374,208; common marmoset cDNA cloned library, 353,664; chimpanzee 22nd chromosome genome library, 13,824; NBRP Xenopus laevis cDNA cloned library, 186,400; NBRP Xenopus tropicalis cDNA cloned library, 44,544; cricket cDNA cloned library, 60,288; *Thermus thermophilus* HB8 expression/KO plasmids, 2,753; *Schizosaccharomyces pombe* cDNA cloned library, (ORFeome library) 14,436; human genome library, 399,456, and *Ciona intestinalis* cDNA cloned library, 452,352.

![Operation of automated DNA-extraction machine](image-url)
2. An E-mail News 34-72 version is sent to users.
3. Number of users registered to RIKEN DNA Bank is 6,651.
4. DNA materials (241,479) have been distributed to users worldwide.
5. The size of the DNA collection archives is now third in the world.
6. The Cre-zoo project was completed in 2008.

II. Technological development
We have performed the following research projects to develop a new technology for DNA Banking.
1. Detection of mutation of DNA samples
   We have developed novel techniques for detecting the mutation of genetic resources with high sensitivities and reproducibilities. These techniques are used for validating the quality of genetic resources.
2. Development of controlled expression system for genes with modification enzymes
   Recent progress in recombinant DNA technology focused on the modification system for genes such as epigenesis, protein degradation, phosphorylation and the addition of sugar and lipid moieties to core proteins and DNAs. We have developed a new two-vector or one-vector system for modifying gene products with genes encoding methylation/demethylation-, kinase/phosphatase-, acetylase/deacetylase-, ubiquitination/deubiquitination-, sumoylation/desumoylation- and sugar/lipid-related enzymes.
3. Development of a system for targeted gene delivery using a specific promoter and generation of transgenic mice with controlled gene expression
   We have developed a regulated gene expression system using reporter constructs of tissue-specific promoters and generated novel transgenic mice with a Cre-loxP cassette with the tissue-specific promoter (in collaboration with Tsukuba University and the Experimental Animal Division of BRC). We are now focusing on the promoters of the p53-targeted gene family.
4. Application of adenovirus vectors to cancer gene therapy, regeneration biology and molecular biology
   We have developed a novel gene delivery system for cancerous cells and embryonic stem cells as well as for model animals using tumor suppressor genes and suicide genes. We have also developed an efficient system for gene transfer using novel adenoviral vectors with E1-Rb mutants, chimeric fibers and modified fibers for gall bladder cancer, biliary tract cancer and liver cancer (in collaboration with Tsukuba University and Sapporo Medical University). We have focused on embryonic stem cells for the gene delivery of modified adenoviral
5. Development of gene expression system and evaluation system of expressed genes in eukaryotic cells and animal models

We have developed a novel strategy for evaluating gene expression in chromatin and for evaluating the system for expressed gene products in cells. We focused on the AP-1 family of transcription factors and on chromatin-modified factors such as those involved in histone acetylation and methylation as well as in sumoylation in eukaryotic cells and model animals.

6. Efficacy of artificial promoter vectors

A controlled reporter system with the DNA binding sites (cis-elements) of transcription factors has been developed and examined of their efficacies for various cells including neoplastic, normal diploid, and embryonic stem cells as well as germ cells.

III. Evaluation of activities of the “National BioResource Project (NBRP; phase I)”.

The NBRP committee evaluated the banking activities of RIKEN BRC with the highest score “S” among those of other groups.

IV. Introduction and distribution of our banking activities

We have set up the homepage http://www.brc.riken.jp/dna/en/index.html and connected with the database of the National Institute of Genetics. We have made e-mail news, catalogs and other related notices of our DNA Bank in RIKEN BRC for researchers worldwide. We have also introduced our banking activities in annual domestic conferences such as those of the Molecular Biology, Biochemistry, Cancer, Gene Therapy, as well as in some international conferences such as the Cold Spring Harbor meetings.
Publications

[Original Papers] (*Peer reviewed journals)


26. Hirano T., Ike F., Murata T., Obata Y., Utiyama H., Yokoyama K.: “Genes encoded within 8q24 on the amplicon of a large extrachromosomal element are selectively repressed during the terminal differentiation of HL-60 cells.” Mutation Research 640, 97-106 (2008).*


Oral Presentations

[International Conferences]


【Domestic Conferences】  Total 60